Translation

PATENT COOPERATION TREATY

PCT/JP2003/007741

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3057WO0P	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP2003/007741	International filing date (*day/month/year*) 18 June 2003 (18.06.2003)	Priority date (*day/month/year*) 19 June 2002 (19.06.2002)
International Patent Classification (IPC) or national classification and IPC A61K 38/17, 31/7088, 39/395, 45/00, 48/00, A61P 19/00, 19/02, 29/00, 43/00 // C12N 15/09		
Applicant TAKEDA CHEMICAL INDUSTRIES, LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24 July 2003 (24.07.2003)	21 April 2004 (21.04.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP2003/007741

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP03/07741

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 16, 17

because:

☒ the said international application, or the said claims Nos. 16, 17 relate to the following subject matter which does not require an international preliminary examination *(specify):*

The subject matter of claims 28 and 36 relates to a method for treatment of the human body by therapy, which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Article 34(4)(a)(i) and Rule 67.1(iv).

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 16, 17.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

As described in the documents listed below, because the use of compounds that inhibit sulfuric ester hydrolases for the prevention and treatment of bone and joint diseases was publicly known before the filing date of this application, the inventions of claims 1-8, 11-15 and 18 and the inventions of claims 9 and 10 are not technically related such that they share the same or a corresponding special technical feature, and therefore they do not constitute one group of inventions so linked as to form a single general inventive concept.

Documents: WO 01/44268 A1 (STERIX LIMITED) June 21, 2001
WO 99/64013 A1 (STERIX LIMITED) December 6, 1999
WO 99/52890 A1 (NOVARTIS AG) October 21, 1999

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1-8, 11-15, 18

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-8, 11-15, 18	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-8, 11-15, 18	NO
Industrial applicability (IA)	Claims	1-8, 11-15, 18	YES
	Claims		NO

2. Citations and explanations

Document 1: WO 01/55411 A2 (MILLENNIUM PHARMACEUTICALS, INC.) August 2, 2001
Document 2: WO 01/44268 A1 (STERIX LIMITED) June 21, 2001
Document 3: WO 99/64013 A1 (STERIX LIMITED) December 6, 1999
Document 4: WO 99/52890 A1 (NOVARTIS AG) October 21, 1999

Document 1 cited in the international search report describes a protein with the same amino acid sequence as SEQ ID NO: 1 of this application (see FIGURES), and it states that this protein is useful in the diagnosis and treatment of sulfatase-related diseases (see page 36, lines 8 to 12), that this polypeptide can be used for screening for substances that act on sulfatases (see page 37, line 16, to page 38, line 29), that antibodies to this polypeptide can be used to treat diseases related to inhibition of sulfatase activity (see page 49, lines 3 to 5), and that antisense nucleotides to the polynucleotides that encode this polypeptide can be designed (see page 58, lines 12 to 13).

Document 2 describes compounds that can inhibit steroid sulfatase activity (see claim 1), and it discloses that these compounds can be useful for the treatment of osteoarthritis, chronic rheumatoid arthritis, osteoporosis, etc. (see page 43, line 28).

Document 3 describes compounds that can be used as estrone sulfatase inhibitors (see Claim 4), and it discloses that these compounds can be useful for the treatment of osteoarthritis, chronic rheumatoid arthritis, osteoporosis, etc. (see page 38, line 31, etc.).

Document 4 describes the use of steroid sulfatase inhibitors in the prevention and treatment of rheumatoid arthritis (see page 14, line 4 from bottom to page 15, line 8).

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

(1) Claims 1-8, 11-15 and 18

The descriptions in the above claims use the term "essentially," but the scope of this term is vague, and these descriptions do not satisfy the requirement for clarity as stipulated in PCT Article 6.

(2) Claims 1, 2, 5, and 18

The above claims describe compounds that inhibit the activity of proteins, etc., having the amino acid sequence identified as SEQ ID NO: 1 and drugs for the prevention and treatment of bone and joint diseases that have, as their active ingredient, compounds that inhibit the expression of the genes for those proteins, etc.

However, it is common technical knowledge that inhibition of the activity and expression of a protein with an elevated level of expression in a specific disease does not guarantee that a preventive or therapeutic effect on that disease will be provided. Therefore, because the Specification of this application describes no pharmacological tests whatsoever on compounds with the above properties, this examination cannot simply conclude that compounds with the above specific inhibitory properties will be effective in the prevention and treatment of bone and joint diseases.

As a result, the inventions of the above claims lack full disclosure in the sense of PCT Article 5 and lack support by disclosure in the Specification in the sense of PCT Article 6.

(3) Claims 3 and 4

The above claims describe antisense polynucleotides to the polynucleotides that encode the proteins, etc., with the amino acid sequence identified as SEQ ID NO: 1 and drugs for the prevention and treatment of bone and joint diseases that have as their active ingredient antibodies to those proteins, etc.

However, the Specification of this application describes no results of pharmacological tests, etc., on the above active ingredient, and therefore for the same reason as stated in (2) above, this examination cannot simply conclude that the above compounds will be effective in the prevention and treatment of bone and joint diseases.

As a result, the inventions of the above claims lack full disclosure in the sense of PCT Article 5 and lack support by disclosure in the Specification in the sense of PCT Article 6.

In addition, even if the general technical knowledge at the time this application was filed is considered, the scope of compounds with the above specific inhibitory properties cannot be identified; therefore the inventions relating to the above claims of this application do not satisfy the requirement for clarity as stipulated in PCT Article 6.

(4) Claims 11-14

The above claims describe a screening method and screening kit for drugs for the prevention of bone and joint diseases that contain proteins, etc., with the amino acid sequence identified as SEQ ID NO: 1 or polynucleotides that encode those proteins.

However, for the same reason as stated in (2) and (3) above, this examination cannot simply conclude that drugs for the prevention and treatment of bone and joint diseases can be obtained by the above method or kit.

As a result the inventions of the above claims lack full disclosure in the sense of PCT Article 5 and lack support by disclosure in the Specification in the sense of PCT Article 6.

(5) Claim 15

The drugs for the preventives/remedies described in the above claim include all preventives/remedies obtained by using the screening method or screening kit described in claims 11-14, but the Specification contains no specific description whatsoever of preventives/remedies obtained by these methods. Therefore, the inventions of these claims lack full disclosure in the sense of PCT Article 5 and lack support by disclosure in the Specification in the sense of PCT Article 6.

In addition, in light of the level of technical knowledge at the time this application was filed, it is unclear which specific substances are included in the scope of this description, and therefore the inventions of the above claims do not satisfy the requirement for clarity as stipulated in PCT Article 6.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

(1) Claims 1-8, 11-15 and 18

The descriptions in the above claims use the term "essentially," but the scope of this term is vague, and these descriptions do not satisfy the requirement for clarity as stipulated in PCT Article 6.

(2) Claims 1, 2, 5, and 18

The above claims describe compounds that inhibit the activity of proteins, etc., having the amino acid sequence identified as SEQ ID NO: 1 and drugs for the prevention and treatment of bone and joint diseases that have, as their active ingredient, compounds that inhibit the expression of the genes for those proteins, etc.

However, it is common technical knowledge that inhibition of the activity and expression of a protein with an elevated level of expression in a specific disease does not guarantee that a preventive or therapeutic effect on that disease will be provided. Therefore, because the Specification of this application describes no pharmacological tests whatsoever on compounds with the above properties, this examination cannot simply conclude that compounds with the above specific inhibitory properties will be effective in the prevention and treatment of bone and joint diseases.

As a result, the inventions of the above claims lack full disclosure in the sense of PCT Article 5 and lack support by disclosure in the Specification in the sense of PCT Article 6.

(3) Claims 3 and 4

The above claims describe antisense polynucleotides to the polynucleotides that encode the proteins, etc., with the amino acid sequence identified as SEQ ID NO: 1 and drugs for the prevention and treatment of bone and joint diseases that have as their active ingredient antibodies to those proteins, etc.

However, the Specification of this application describes no results of pharmacological tests, etc., on the above active ingredient, and therefore for the same reason as stated in (2) above, this examination cannot simply conclude that the above compounds will be effective in the prevention and treatment of bone and joint diseases.

As a result, the inventions of the above claims lack full disclosure in the sense of PCT Article 5 and lack support by disclosure in the Specification in the sense of PCT Article 6.

(4) Claims 11-14

The above claims describe a screening method and screening kit for drugs for the prevention of bone and joint diseases that contain proteins, etc., with the amino acid sequence identified as SEQ ID NO: 1 or polynucleotides that encode those proteins.

However, for the same reason as stated in (2) and (3) above, this examination cannot simply conclude that drugs for the prevention and treatment of bone and joint diseases can be obtained by the above method or kit.

As a result the inventions of the above claims lack full disclosure in the sense of PCT Article 5 and lack support by disclosure in the Specification in the sense of PCT Article 6.

(5) Claim 15

The drugs for the preventives/remedies described in the above claim include all preventives/remedies obtained by using the screening method or screening kit described in claims 11-14, but the Specification contains no specific description whatsoever of preventives/remedies obtained by these methods. Therefore, the inventions of these claims lack full disclosure in the sense of PCT Article 5 and lack support by disclosure in the Specification in the sense of PCT Article 6.

In addition, in light of the level of technical knowledge at the time this application was filed, it is unclear which specific substances are included in the scope of this description, and therefore the inventions of the above claims do not satisfy the requirement for clarity as stipulated in PCT Article 6.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V:

oClaims 1-8, 11-15 and 18

Documents 1-4 above do not describe the inventions of claims 1-8, 11-15 and 18, and therefore these inventions are novel.

When we compare the inventions of the claims of this application with the invention described in document 1, whereas the target of the active ingredient is identified as bone and joint diseases in the inventions of the claims of this application, in the invention described in document 1 it is identified only as "sulfatase-related diseases" and document 1 does not clearly state that bone and joint diseases are the target. In this respect, the two differ.

However, documents 2-4 state that compounds that inhibit sulfatase activity can be used to treat bone and joint diseases such as osteoarthritis, chronic rheumatoid arthritis, osteoporosis, etc., and based on this description, this examination considers bone and joint diseases to be "sulfatase-related diseases," and persons skilled in the art can easily use the active ingredient for the treatment of the above bone and joint diseases in the invention described in document 1.

In addition, this examination finds that no particularly outstanding effect is provided thereby.

As a result, the inventions of claims 1-8, 11-15 and 18 lack an inventive step with respect to documents 1-4.